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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,923	11/25/2003	Qing Wang	ROGO 217 (10309708)	9786

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FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,923	WANG ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RP

DETAILED ACTION

Amendment Entry and Claim Status

The amendment filed on March 3, 2005 has been acknowledge and entered and the supplemental amendment filed on May 10, 2005 has been acknowledged and entered.

Claims 1-9 were cancelled.

Claims 10-17 are pending.

Withdrawn Rejection(s)

Rejection under 35 USC 112, 2nd paragraph is withdrawn herein.

Rejections under 35 USC 102 and 103 for claims 1-9 in the previous office action are withdrawn herein.

New Ground of Rejection(s)

Specification Objections

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: support for 2-aminothiolane-HCl is required in the specification. The specification fails to describe 2-aminothiolane-HCl. On page 4, paragraph 3, describes the use of Traut's reagent , 2-iminothilane-HCl but fails to describe 2-aminothiolane-HCl. According to the prior arts, aminothiolane and iminothiolane are both known as Traut's reagent (see Calias et al. 6,749,865, col. 5, lines 10-13). If iminothiolane and aminothiolane are meant to be the same or used interchangeably, please also verify.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is unclear of whether "a ligand" in line 1 and "a ligand" in line 6 are the same or different. Please verify.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Bieniarz et al.(US 5,063,109).

Bieniarz teaches a method of attaching a ligand to a solid phase comprising contacting an amine microparticles with 2-iminothiolane HCl (a molecule which reacts with amine); reacting a conjugate comprising maleimide derivatized antibodies (linker-ligand) with said iminothiolane HCL-solid phase to attach the ligand to the microparticles. (see examples 7 & 16, especially col. 13, lines 33-40). Regarding the limitation of the molecule contains a protected or unprotected sulfhydryl group: since Bieniarz teaches the same molecule as of the present invention, such molecule must

contain a protected or unprotected sulfhydryl group and must also react with the amine group in an acylation reaction. Since aminothiolane is known in the art as a Traut's reagent (see Calias 6,749,865) and iminothiolane is described in the present specification as a Traut's reagent, both must be the same and used interchangeably. Bieniarz also teaches that 2-iminothiolane-HCl is contacted to said surface of the solid phase (particle) in a solution consisting of dimethyl formamide (DMF). In example 16, the particles are treated with 2-imithiolane-HCl and then are mixed with a volume of compound 3 solution in DMF. (see examples 7 and 16).

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Pope et al. (US 5,399,501).

Pope teaches a method for attaching a ligand to a solid phase comprising: contacting an amine group on the surface of a solid phase with a molecule comprising a thiol introducing agent such as thiolanes, succinimidyl thioacetates such as N-succinimidyl-S-acetylthioacetate, and disulfide compounds which are subsequently reduced to a thiol. The specific binding member is activated by a maleimido-NHS active ester heterobifunctional reagent to incorporate a thiol-reactive group on the protein. The derivatized specific binding member is then added to the thiolated solid phase and reacted to produce a covalent linkage. Regarding claim 8, since Pope teaches the same molecule, i.e. thiolanes or succinimidyl thioacetates, such molecule would react with the amine group on the solid phase via an acylation reaction. Pope's solid phase with a ligand attached thereto satisfies the requirement of claim 9. The specific binding pair member includes that binds with the analyte , which are protein, peptide, an amino acid,

and a drug, include those administered for therapeutic purposes, a bacterium, a virus, and metabolites. The solid phase include polymeric or glass beads, microparticles, tubes, sheets, plates, etc. (see col. 6, lines 8-52; col. 7, lines 27-60; col. 8, lines 16-68; col. 9, line 49-col. 10, line 15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14 & 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz in view of Hansen et al. (US 6,663,861).

Bieniarz has been discussed above.

However, Bieniarz fails to teach a linker as p-maleimidophenyl isocyanate and contacting the surface with a 2-aminothiolane HCl, followed by contacting a sulfhydryl group provided by 2-aminothiolane-HCl with p-maleimido phenyl isocyanate.

Hansen teaches various methods of covalent coupling such as coupling a molecule with sulfhydryl groups to hydroxyl groups by using a N-(p-maleimidophenyl) isocyanate. (see col. 5, lines 15-25).

It would have been obvious to one of ordinary skills in the art to use N-(p-maleimidophenyl) isocyanate as a linker as suggested by Hansen to link the ligand which contains a hydroxyl group to 2-iminothiolane-HCl also known as 2-aminothiolane-HCl or Traut's reagent, which contains a sulfhydryl group as taught in the method of

Bieniarz since Bieniarz teaches using a maleimide for linking the ligand which contains a hydroxyl group and a sulfhydryl group. N-(p-maleimidophenyl) isocyanate is known as a heterobifunctional crosslinker which links a ligand to a solid surface.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pope et al. (US 5,399,501) in view of Hansen et al. (US 6,663,861).

Pope has been discussed above for teaching a method of attaching a ligand to a solid phase comprising contacting an amine group on the surface of the solid phase with a molecule comprising a thiol introducing agent such as thiolanes, succinimidyl thioacetates such N-succinimidyl-S-acetylthioacetate and disulfide compounds which are subsequently reduced to a thiol.

However, Pope fails to teach contacting the sulfhydryl group produced by the molecule comprising a thiol introducing agent on the surface of the solid phase with p-maleimidophenyl isocyanate.

Hansen has been discussed above for teaching various methods of covalent coupling such as coupling a molecule with sulfhydryl group to hydroxyl groups by using a N-(p-maleimidophenyl) isocyanate. (see col. 5, lines 15-25).

It would have been obvious to one of ordinary skills in the art to use N-(p-maleimidophenyl) isocyanate as a linker as suggested by Hansen to link the ligand contains a hydroxyl group to 2-iminothiolane-HCl also known as 2-aminothiolane-HCl or Traut's reagent, which contains sulfhydryl group as taught by Pope since Pope teaches using a maleimido-NHS active ester heterobiofunctional reagent to incorporate a thio-reactive group on the ligand/protein that contains a hydroxyl group and a sulfhydryl

group. N-p-maleimidophenyl isocyanate is known as a heterobiofunctional crosslinker which links the ligand to a solid phase.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz (US 5,063,109) in view of Siiman et al. (US 5,639,620).

Bieniarz has been discussed above.

However, Bieniarz fails to teach magnetic particles being the solid phase.

Siiman teaches magnetic particles coated with aminodextran or gelatin which contains an amine pendent group. Crosslink the ligand/protein/antibody with the magnetic particles by using the bifunctional crosslinking agent such as p-iminothiolane hydrochloride. The coupling of the biological substance to the particle involves activation of the free amino groups of the gelatin-coated particles with water soluble heterobifunctional reagent such as 2-iminothiolane hydrochloride (IT) also known as 2-aminothiolane-HCl or Traut's reagent, sulfosuccinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate (sulfo-SMCC), m-maleimidobenzoyl-N-hydroxysuccinimide ester, N-succinimidy1-3-(2-pyridyldithio)propionate, succinimidyl-4-(p-maleimidophenyl)butyrate, N-succinimidyl-(4-iodoacetyl)aminobenzoate, the reagents listed above as substitutes for glutaraldehyde and the like. The 2-iminothiolane hydrochloride also known as 2-aminothiolane-HCl or Traut's reagent and the maleimidyl/succinimidyl reagents are preferred. (see col. 7, lines 60-65; col. 10, lines 15-25, 53-60)

It would have been obvious to one of ordinary skills in the art to use magnetic particles as a solid phase as taught by Siiman in the method of Bieniarz since both

references teach a method of conjugating a ligand to a solid surface via a bifunctional crosslinking agent and because ligand bound magnetic particles, in an immunoassay, can be separated by magnetic force rather than centrifugation which is time consuming.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pope et al. (US 5,399,501) in view of Armstrong (US 5,964,996).

Pope has been discussed above.

However, Pope fails to teach the ligand is an antibiotic.

Armstrong teaches macrocyclic antibiotic chemically bonded to a solid support such as silica gel, agarose, dextran, cellulose, branch amylose (see col. 6, lines 58-67; col. 7, lines 5-10). via linkages such as amine, amide, thioler groups (see col. 7, lines 27-30).

It would have been obvious to one of ordinary skills in the art to attach antibiotic as taught by Armstrong to solid phase according to the method of Pope through routine experimentation since these antibiotics also contain a carboxyl or thiolether groups thereby enabling the reaction with a coupling agent or thiol introducing agent.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pope et al. (US 5,399,501) in view of Armstrong (US 5,964,996) further in view of Molna-Kimber et al. (US Patent Application Publication 2002/0151088A1).

Pope and Armstrong have been discussed above.

Both Pope and Armstrong fail to teach antibiotic such as Rapamycin.

Molna-Kimber teaches rapamycin is a macrocylic antibiotic. (see page 1, 1st col. 2nd paragraph).

It would have been obvious to one of ordinary skills to use Rapamycin as taught by Molna-Kimber in the combination method of Pope and Armstrong since Rapamycin is a macrocyclic antibiotic and Pope in combination with Armstrong suggested that macrocylic antibiotics can be coupled to a solid phase for detecting specific antibodies against antibiotics such as Rapamycin because Rapamycin have immunosuppressant activity as well as antibiotic and other pharmacological activities and are useful in treating graft and transplant rejections, diseases of inflammation and autoimmune diseases such as rheumatoid arthritis, diabetes, and multiple sclerosis.

Response to Arguments

Applicant's arguments filed March 3, 2005 have been fully considered but they are not persuasive.

Applicants argue that Bieniarz fails to teach a sulphur moiety resulting from the reaction of the first and second molecules. Applicants also mention that example 16 discusses the use of iminothiolane HCl which contains a sulfhydryl group; however, the reaction with "compound 3" results in the removal of the sulfhydryl group. Thus, without the sulfhydryl group, the reference fails to anticipate the claimed invention.

Examples 7 & 16 of Bieniarz does not mention anything about the removal of the sulfhydryl group when reacted with "compound 3". Until Applicants show proof and support for this "removal" of the sulfhydryl group when reacted with "compound 3", Bieniarz still applies to the claimed invention.

Regarding the Pope reference, Applicants argue that because Pope requires an additional step to incorporate sulfhydryl group, as compared to the claimed invention, Pope fails to teach that the solid phase contains a sulfhydryl group.

Because the present claims contain an open claim language, i.e. comprising, they fail to exclude additional method step such as adding DTT in excess.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
May 6, 2005

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
5/11/05